

REMARKS

This Amendment is filed in response to the Final Office Action dated January 22, 2009, and is respectfully submitted to be fully responsive to the rejections raised therein. Accordingly, favorable reconsideration on the merits and allowance are respectfully requested.

In the present Amendment, claim 1 has been amended by incorporating the subject matter recited in claims 2 and 4 and by inserting that the infusion preparation comprises about 0.01 mg to about 20 mg of (2R)-2-propyloctanoic acid or a salt thereof. Support for the amendments can be found, e.g., in original claims 2 and 4 and in the specification in the paragraph bridging pages 21-22.

Claims 2, 4, and 13 have been canceled.

Claims 5 and 6 have been amended to depend from claim 1.

Claims 14 and 15 have been withdrawn.

Claim 16 was canceled previously.

Claims 3 and 9 are amended to improve their form.

No new matter has been added. Entry of the Amendment is respectfully submitted to be proper. Upon entry of the Amendment, claims 1, 3, 5, 6-12 and 14-15 will be all the claims pending in the application.

II. Rejection Under 35 U.S.C. § 103(a)

Claims 1-13 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent 6,608,221 (Toda) in view of U.S. Patent 6,043,223 (Black) or U.S. 2003/0104079 (Sakanaka) for the reasons of record, as provided in the previous Office Action dated April 15, 2008. Specifically, the Examiner's position is that Toda teaches a composition² comprising (2R)-2-propyloctanoic acid.³ Examiner Sznajdman concedes that Toda fails to disclose an infusion preparation. Per the Examiner, preparations of infusions are well known in the art, as taught by Black.⁴ Thus, according to the Examiner, it would have been *prima facie* obvious for a person of ordinary skill in the art to prepare an infusion of a known product based on the teachings the prior art references.

The Examiner asserts that the present invention is obvious from the combination of (2R)-2-propyloctanoic acid, disclosed by Toda, and the infusion preparation of bradykinin disclosed by Black or the intravenous infusion comprising ginsenosides disclosed by Sakanaka. Additionally, the Examiner asserts that an infusion preparation of (2R)-2-propyloctanoic acid can be produced even though the structures of bradykinin and ginsenosides are structurally different from (2R)-2-propyloctanoic acid as recited in the present claimed invention.

Applicants traverse and respectfully request reconsideration in view of the amendments to the claims and the following remarks.

² The Examiner asserts that Toda teaches "a composition", but Toda is directed to the compound (2R)-2-propyloctanoic acid and the process of making the same.

³ Office Action dated April 15, 2008, page 4.

⁴ *Id.*

Amended claim 1 recites an infusion preparation comprising about 0.01 mg to about 20 mg of (2R)-2-propyloctanoic acid or a salt thereof per mL and about 1 to 5 equivalents of a basic metal ion based on 1 equivalent of (2R)-2-propyloctanoic acid or a salt thereof, which infusion preparation comprises at least one selected from a metal salt of phosphoric acid, a metal salt of carbonic acid, a metal salt of sulfurous acid, a metal salt of organic sulfonic acid and a metal salt of organic C2-6 carboxylic acid, and optionally further comprises a metal hydroxide, as a source(s) of the basic metal ion.

The infusion preparation of the present invention cannot be prepared easily even if the teachings of Black or Sakanaka are combined with (2R)-2-propyloctanoic acid disclosed by Toda. The Examiner asserts that Black describes an infusion preparation of bradykinin containing sodium hydroxide and PBS (phosphate buffered saline). In lines 47-62 in column 5 in Black, Black discloses that the bradykinin/bradykinin analog and zaprinast are preferably infused in the form of a pharmaceutical solution having a 0.09 % PBS solution as the carrier; that the concentration of bradykinin/bradykinin analog in the solution is 10-40 µg/ml with the preferred concentration of zaprinast being on order of 1 to 10 mg/ml for carotid artery administration; and that for intravenous administration, the concentration of bradykinin/bradykinin analog is preferably between about 15 µg/ml to 50 mg/ml with the preferred concentration of zaprinast being on the order of 2 to 15 mg/ml.

Additionally, the infusion preparation for a pharmaceutical solution is prepared by dissolving zaprinast in 1 M sodium hydroxide to form a concentrated solution of approximately 100 to 500 mg/ml zaprinast, since zaprinast, which is a cyclic GMP phosphodiesterase inhibitor, is not soluble directly in saline. The concentrated solution is then dissolved into phosphate

buffered saline (PBS) to the final desired concentration. The bradykinin or the bradykinin analog is then added to the solution to form the final pharmaceutical preparation. Finally, the relative concentrations within the pharmaceutical preparation are adjusted as set forth above to provide a solution which is suitable for either carotid artery infusion or intravenous administration.

Namely, in case of infusion preparation for intravenous administration, the infusion preparation of bradykinin disclosed by Black is a prepared comprising:

- (1) 15 µg/ml to 50 mg/ml bradykinin/bradykinin analog,
- (2) 2 to 15 mg/ml zaprinast,
- (3) 4 to 150 mM sodium hydroxide which is used for dissolving zaprinast and
- (4) 0.09% PBS. Since molecular weight of bradykinin is 1060, 15 µg/ml to 50 mg/ml corresponds to 0.014 mM to 47.17 mM.

On the other hand, the amount of a basic metal ion included in 0.09% PBS is fixed and 0.016 mM. Therefore, the infusion preparation of bradykinin taught by Black contains from 0.085 equivalents to 10715 equivalents of a basic metal ion based on 1 equivalent of bradykinin. Therefore, it is predictable to choose about 1 to about 5 equivalents of a basic metal ion from a extremely broad range spanning more than 120,000 equivalents, or it is not obvious to try the whole range from 0.085 equivalents to 10715 equivalents, and therefore the presently claimed infusion preparation is not obvious.

Additionally, almost all of a basic metal ion in infusion preparation of Black is derived from sodium hydroxide used for dissolving zaprinast and is not added for avoiding clouding.

On the other hand, in paragraph [0235] in Sakanaka, as pointed out by the Examiner, dihydroginsenoside derivative can be used as intravenous infusion preparation after being dissolved in physiological saline, distilled water, phosphate buffer, glucose solution, liposome or fat emulsion. In this connection, there is no description in the specification of the concentration of phosphate buffer. However, in view of the object of using an infusion preparation is to directly administer the preparation to a living body, the person skilled in the art would use isotonic solution, namely, 0.067 M phosphate buffer solution. The 0.067 M phosphate buffer solution is 0.067 M solution prepared by mixing same amount of KH_2PO_4 and K_2HPO_4 in which concentration of phosphate (PO_4) ion is 0.067 M. Thus, a basic ion metal derived from the solution is three times of the concentration of phosphate ion, namely, 0.201 M.

The preparation disclosed by Sakanaka is a pharmaceutical composition of low dose and low concentration comprising ginsenosides or salts thereof in an amount of less than 0.001 % by weight or less (U.S. 2003/0104079A1, paragraph [0020]). For example, in composition (infusion preparation) comprising 0.001 % by weight of ginsenosides, the concentration is 0.009 mM since the molecular weight of ginsenoside Rb_1 is about 1109.

Therefore, in infusion preparation of ginsenosides disclosed in Sakanaka, 22333 equivalents of basic metal ion is included based on 1 equivalent of ginsenosides. From such scope, it is not easy to expect only about 1 to about 5 equivalents as recited in the present claimed invention.

Furthermore, it is disclosed in Black and/or Sakanaka that the same carrier can be used for any amount of active ingredients. On the other hand, in the present invention, clouding

problem can be solved by changing amount of the basic metal ion according to amount of basic metal ion.

In view of the above, the present claimed invention cannot be accomplished based on the teachings of Toda alone or in combination with Black and Sakanaka. Therefore, the present application is not obvious from these publications.

II. Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

/Sunhee Lee/

Sunhee Lee
Registration No. 53,892

SUGHRUE MION, PLLC
Telephone: (202) 293-7060
Facsimile: (202) 293-7860

WASHINGTON DC SUGHRUE/265550

65565

CUSTOMER NUMBER

Date: May 21, 2009

Respectfully submitted,

/Nyeemah A. Grazier/

Nyeemah A. Grazier
Registration No. 63,657